PATENT COOPERATION TREATY

From the
INTERNATIONAL PRELIMINARY EXAMINING AUTHORITY

To:

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PCT

NOTIFICATION OF TRANSMITTAL OF THE INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

(PCT Rule 71.1)

Date of mailing *(day/month/year)*	08.12.2005

Applicant's or agent's file reference	IMPORTANT NOTIFICATION
A3013-PCT	

International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/EP2004/010198	13.09.2004	12.09.2003

Applicant
4 AZA BIOSCIENCE NV

1. The applicant is hereby notified that this International Preliminary Examining Authority transmits herewith the international preliminary report on patentability and its annexes, if any, established on the international application.

2. A copy of the report and its annexes, if any, is being transmitted to the International Bureau for communication to all the elected Offices.

3. Where required by any of the elected Offices, the International Bureau will prepare an English translation of the report (but not of any annexes) and will transmit such translation to those Offices.

4. **REMINDER**

The applicant must enter the national phase before each elected Office by performing certain acts (filing translations and paying national fees) within 30 months from the priority date (or later in some Offices) (Article 39(1)) (see also the reminder sent by the International Bureau with Form PCT/IB/301).

Where a translation of the international application must be furnished to an elected Office, that translation must contain a translation of any annexes to the international preliminary report on patentability. It is the applicant's responsibility to prepare and furnish such translation directly to each elected Office concerned.

For further details on the applicable time limits and requirements of the elected Offices, see Volume II of the PCT Applicant's Guide.

The applicant's attention is drawn to Article 33(6), which provides that the criteria of novelty, inventive step and industrial applicability described in Article 33(2) to (4) merely serve the purposes of international preliminary examination and that "any Contracting State may apply additional or different criteria for the purposes of deciding whether, in that State, the claimed inventions is patentable or not" (see also Article 27(5)). Such additional criteria may relate, for example, to exemptions from patentability, requirements for enabling disclosure, clarity and support for the claims.

Name and mailing address of the international preliminary examining authority:	Authorized Officer
European Patent Office - P.B. 5818 Patentlaan 2 NL-2280 HV Rijswijk - Pays Bas Tel. +31 70 340 - 2040 Tx: 31 651 epo nl Fax: +31 70 340 - 3016	Lafitte-de Jong, S Tel. +31 70 340-4827

PATENT COOPERATION TREATY

PCT

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

(Chapter II of the Patent Cooperation Treaty)

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference A3013-PCT	**FOR FURTHER ACTION**	See Form PCT/IPEA/416
International application No. PCT/EP2004/010198	International filing date *(day/month/year)* 13.09.2004	Priority date *(day/month/year)* 12.09.2003
International Patent Classification (IPC) or national classification and IPC A61K31/519, A61K31/5377, A61K31/541, A61P29/00, A61P31/00, A61P39/00, A61P3/00, A61P25/28, A61P35/02, A61P1/16		
Applicant 4 AZA BIOSCIENCE NV		

1. This report is the international preliminary examination report, established by this International Preliminary Examining Authority under Article 35 and transmitted to the applicant according to Article 36.
2. This REPORT consists of a total of 9 sheets, including this cover sheet.
3. This report is also accompanied by ANNEXES, comprising:
   a. ☒ *sent to the applicant and to the International Bureau)* a total of 7 sheets, as follows:
      ☒ sheets of the description, claims and/or drawings which have been amended and are the basis of this report and/or sheets containing rectifications authorized by this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions).
      ☐ sheets which supersede earlier sheets, but which this Authority considers contain an amendment that goes beyond the disclosure in the international application as filed, as indicated in item 4 of Box No. I and the Supplemental Box.
   b. ☐ *(sent to the International Bureau only)* a total of (indicate type and number of electronic carrier(s)) , containing a sequence listing and/or tables related thereto, in computer readable form only, as indicated in the Supplemental Box Relating to Sequence Listing (see Section 802 of the Administrative Instructions).

4. This report contains indications relating to the following items:

   ☒ Box No. I Basis of the opinion
   ☒ Box No. II Priority
   ☒ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
   ☒ Box No. IV Lack of unity of invention
   ☒ Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
   ☐ Box No. VI Certain documents cited
   ☒ Box No. VII Certain defects in the international application
   ☒ Box No. VIII Certain observations on the international application

Date of submission of the demand	Date of completion of this report
12.07.2005	08.12.2005
Name and mailing address of the international preliminary examining authority: European Patent Office - P.B. 5818 Patentlaan 2 NL-2280 HV Rijswijk - Pays Bas Tel. +31 70 340 - 2040 Tx: 31 651 epo nl Fax: +31 70 340 - 3016	Authorized Officer Cielen, E Telephone No. +31 70 340-4540

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

International application No.
PCT/EP2004/010198

Box No. I Basis of the report

1. With regard to the **language**, this report is based on the international application in the language in which it was filed, unless otherwise indicated under this item.

   ☐ This report is based on translations from the original language into the following language , which is the language of a translation furnished for the purposes of:
   - ☐ international search (under Rules 12.3 and 23.1(b))
   - ☐ publication of the international application (under Rule 12.4)
   - ☐ international preliminary examination (under Rules 55.2 and/or 55.3)

2. With regard to the **elements*** of the international application, this report is based on *(replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report)*:

Description, Pages

1-58	as originally filed

Claims, Numbers

1-7	filed with telefax on 28.10.2005

Drawings, Sheets

1/7-7/7	as originally filed

☐ a sequence listing and/or any related table(s) - see Supplemental Box Relating to Sequence Listing

3. ☒ The amendments have resulted in the cancellation of:
   - ☐ the description, pages
   - ☒ the claims, Nos. 8-12
   - ☐ the drawings, sheets/figs
   - ☐ the sequence listing *(specify)*:
   - ☐ any table(s) related to sequence listing *(specify)*:

4. ☐ This report has been established as if (some of) the amendments annexed to this report and listed below had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).
   - ☐ the description, pages
   - ☐ the claims, Nos.
   - ☐ the drawings, sheets/figs
   - ☐ the sequence listing *(specify)*:
   - ☐ any table(s) related to sequence listing *(specify)*:

* *If item 4 applies, some or all of these sheets may be marked "superseded."*

INTERNATIONAL PRELIMINARY REPORT ON PATENTABILITY

International application No.
PCT/EP2004/010198

Box No. II Priority

1. ☒ This report has been established as if no priority had been claimed due to the failure to furnish within the prescribed time limit the requested:
   - ☒ copy of the earlier application whose priority has been claimed (Rule 66.7(a)).
   - ☐ translation of the earlier application whose priority has been claimed (Rule 66.7(b)).
2. ☐ This report has been established as if no priority had been claimed due to the fact that the priority claim has been found invalid (Rule 64.1). Thus for the purposes of this report, the international filing date indicated above is considered to be the relevant date.
3. Additional observations, if necessary:

Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1. The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been examined in respect of:

   ☐ the entire international application,

   ☒ claims Nos. 1-6 (all partially)

   because:

   ☐ the said international application, or the said claims Nos. relate to the following subject matter which does not require an international preliminary examination (specify):

   ☐ the description, claims or drawings *(indicate particular elements below)* or said claims Nos. are so unclear that no meaningful opinion could be formed *(specify)*:

   ☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.

   ☒ no international search report has been established for the said claims Nos. 1-6 (all partially)

   ☐ the nucleotide and/or amino acid sequence listing does not comply with the standard provided for in Annex C of the Administrative Instructions in that:

the written form	☐	has not been furnished
	☐	does not comply with the standard
the computer readable form	☐	has not been furnished
	☐	does not comply with the standard

   ☐ the tables related to the nucleotide and/or amino acid sequence listing, if in computer readable form only, do not comply with the technical requirements provided for in Annex C-*bis* of the Administrative Instructions.

   ☐ See separate sheet for further details

Box No. IV Lack of unity of invention

1. ☒ In response to the invitation to restrict or pay additional fees, the applicant has:
   - ☐ restricted the claims.
   - ☒ paid additional fees.
   - ☐ paid additional fees under protest.
   - ☐ neither restricted nor paid additional fees.

2. ☐ This Authority found that the requirement of unity of invention is not complied with and chose, according to Rule 68.1, not to invite the applicant to restrict or pay additional fees.

3. This Authority considers that the requirement of unity of invention in accordance with Rules 13.1, 13.2 and 13.3 is

   ☐ complied with.

   ☐ not complied with for the following reasons:

4. Consequently, this report has been established in respect of the following parts of the international application:

   ☒ all parts.

   ☐ the parts relating to claims Nos. .

Box No. V Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes:	Claims	1-7
	No:	Claims	-
Inventive step (IS)	Yes:	Claims	1-7
	No:	Claims	-
Industrial applicability (IA)	Yes:	Claims	1-7
	No:	Claims	

2. Citations and explanations (Rule 70.7):

see separate sheet

Box No. VII Certain defects in the international application

The following defects in the form or contents of the international application have been noted:

see separate sheet

Box No. VIII Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the question whether the claims are fully supported by the description, are made:

see separate sheet

Re Item I

Basis of the report

The amendments filed with the telefax dated 28.10.2005 are in accordance with Article 34(2)(b) PCT. See, however, item **VII**.

Re Item III

Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

III.i. Present claims 1-6 relate to a large number of possible compounds, namely "a dihydro- or tetrahydropteridine derivative thereof". Support within the meaning of Article 6 PCT and disclosure within the meaning of Article 5 PCT is to be found, however, for only a small proportion of the compounds claimed. In the present case, the claims so lack support, and the application so lacks disclosure, that a meaningful search over the whole of the claimed scope is impossible. Consequently, the search has been carried out for those parts of the claims which appear to be supported and disclosed, namely those parts relating to the compounds of general formula (I) and/or a pharmaceutically acceptable addition salt thereof and/or a stereoisomer thereof and/or a mono- or a di-N-oxide thereof and/or a solvate thereof and the compounds specifically mentioned in claim 7, with due regard to the general idea underlying the application.

III.ii. No opinion will be given in respect of subject-matter which is not covered by the search report (Rule 66.1(e) PCT) (see also item **V.i**).

Re Item IV

Lack of unity of invention

For the claims as originally filed, a lack of unity objection within the meaning of Rule 13.1 PCT was raised. As the Applicant has had a search report drawn up on all inventions, **the application will be prosecuted on the basis of the inventions in respect of which a search has been carried out, in other words all inventions as originally defined, i.e. present claims 1-7.**

Re Item V

Reasoned statement with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

V.i. Attention is drawn to the fact that the present statement expressed as to novelty, inventive step and industrial applicability refers only to matter for which an International Search Report has been drawn up (i.e. only for the use of the compounds of general formula (I) and/or a pharmaceutically acceptable addition salt thereof and/or a stereoisomer thereof and/or a mono- or a di-N-oxide thereof and/or a solvate thereof and the compounds specifically mentioned in claim 7 for the prevention or treatment of toxic effects of TNF-alpha, alcohol-induced hepatitis and cachexia, with due regard to the general idea underlying the application).

V.ii. Article 33(2) PCT.

The present application meets the criteria of Article 33(1) PCT, because the subject-matter of claims 1-7 is new in the sense of Article 33(2) PCT.

None of the cited prior art documents discloses the use of the presently claimed pteridine derivatives of formula (I) for the treatment of toxic effects of TNF-alpha, alcohol-induced hepatitis or cachexia.

V.iii. Article 33(3) PCT.

(a) The problem to be solved by the present application is the provision of alternative medicines for the prevention or treatment of TNF-alpha mediated disorders, selected from the group consisting of toxic effects of TNF-alpha, alcohol-induced hepatitis or cachexia.

The proposed solution is the use of pteridines of general formula (I).

(b) Bearing in mind items **III.ii** and **V.i**, the use of compounds of present formula (I) for the prevention or treatment of toxic effects of TNF-alpha, cachexia and alcohol-induced hepatitis may appear inventive in the light of the cited prior art.

The presently disclosed data only relate to (1) TNF-alpha inhibition (example 195), (2)

protection against lethal toxic shock (example 196), (3) protection against a lethal dose of TNF-alpha and (4) reduction of tumor growth while reducing TNF-alpha toxicity, by the compounds of general formula (I).

However, an inventive step for the treatment or prevention of cachexia and alcohol-induced hepatitis appears to be present since the involvement of TNF-alpha in each of these diseases was already known before the date of the application (documents not shown).

Re Item VII

Certain defects in the international application

VII.i. Several compounds of claim 7 do not fit in claim 1 because of the substituents on the phenyl group in position 6. Claim 7 should therefore partially have been drafted as an independent claim.

VII.ii. Equally, due to the amendments made for the substituents R_4 and R_3 in formula (I) (claim 1), several of the embodiments of claim 4 cannot be dependent on claim 1 any more.

Re Item VIII

Certain observations on the international application

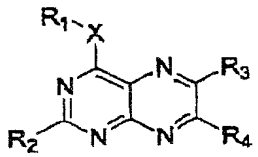
Claims 1-6 of the present application relate to a wide variety of compounds which all are supposed to be effective as medicaments for preventing or treating toxic effects of TNF-alpha, alcohol-induced hepatitis or cachexia. In fact, as far as the embodiment "and/or a dihydro- or tetrahydropteridine derivative thereof" is concerned, these claimed variants appear to be disproportionate to what actually is disclosed and supported by pharmacological evidence, as no synthetic or pharmacologic example of such a compound could be found in the application.

As a rule, protection conferred by a patent should be commensurate with the range of compounds for which the effect has been properly demonstrated, including obvious variants thereof. This appears not to be the case here; therefore the present application as it stands falls foul of the clear provisions of Article 6 PCT (see also item **III.i**).

CLAIMS

1. Use of a pteridine derivative for the manufacture of a medicament for the prevention or treatment of a disorder in a mammal, the said disorder being selected from the group consisting of toxic effects of TNF-α, alcohol-induced hepatitis, and cachexia,

the said pteridine derivative having the general formula (I):



wherein X represents an oxygen atom or a group with the formula $S(O)_m$ wherein m is an integer from 0 to 2, or a group with the formula NZ and wherein:

- R_1 is selected from the group consisting of methyl, ethyl, isopropyl and pentyl;
- Z is a group independently defined as R_1 or Z is hydrogen or the group NZ together with R_1 is either hydroxylamino or an optionally substituted heterocyclic group containing at least one nitrogen atom;
- R_2 is selected from the group consisting of amino; acylamino;
- R_4 is an atom or a group selected from the group consisting of hydrogen; halogen; C_{1-7} alkyl; C_{2-7} alkenyl; C_{2-7} alkynyl; halo C_{1-7} alkyl; carboxy C_{1-7} alkyl; acetoxy C_{1-7} alkyl; carboxyaryl; C_{1-7} alkoxy; C_{3-10} cycloalkoxy; aryloxy; arylalkyloxy; oxyheterocyclic; heterocyclic-substituted alkyloxy; thio C_{1-7} alkyl; thio C_{3-10} cycloalkyl; thioaryl; thioheterocyclic; arylalkylthio; heterocyclic-substituted alkylthio; amino; hydroxylamino; mercapto-amino; acylamino; thioacylamino; alkoxyamino; thioalkylamino; acetal; thioacetal; carboxylic acid; carboxylic acid esters, thioesters, halides, anhydrides, amides and thioamides; thiocarboxylic acid; thiocarboxylic acid esters, thioesters, halides, anhydrides, amides and thioamides; hydroxyl; sulfhydryl; nitro; cyano; carbamoyl; thiocarbamoyl, ureido; thio-ureido; alkylamino; cycloalkylamino; alkenylamino; cycloalkenylamino; alkynyl-amino; arylamino; arylalkylamino; hydroxyalkylamino; mercapto-alkylamino; heterocyclic amino; heterocyclic-substituted alkylamino; oximino; alkyloximino; hydrazino; alkylhydrazino; phenylhydrazino; cysteinyl acid, esters, thioesters, halides, anhydrides, amides and thioamides thereof; aryl groups optionally substituted with one or more substituents selected from the group consisting of halogen, C_{1-7} alkyl, C_{1-7} alkoxy; optionally substituted heterocyclic radicals; aromatic or heterocyclic substituents substituted with an aliphatic spacer between the pteridine ring and the aromatic or heterocyclic substituent, whereby said aliphatic spacer is a branched or straight, saturated or unsaturated aliphatic chain of 1 to 4 carbon atoms; branched or straight, saturated or unsaturated aliphatic chains of 1 to 7 carbon atoms; and

- R_3 is an atom or a group defined as R_4, or R_3 together with R_4 forms a homocyclic or heterocyclic radical;

and/or being a pharmaceutically acceptable addition salt thereof and/or a stereoisomer thereof and/or a mono- or a di-*N*-oxide thereof and/or a solvate and/or a dihydro- or tetrahydropteridine derivative thereof.

2. Use according to claim 1, wherein R_4 is hydrogen or methoxy.

3. Use according to claim 1, wherein R_3 is 3-thienyl, 2-thienyl or a phenyl group with one or more substituents.

4. Use according to claim 1, wherein R_3 is a phenyl group with one or more substituents each independently selected from the group consisting of fluoro, methoxy, ethoxy, trifluoromethyl, dimethylamino, chloro, cyano, methyl, ethyl, carboxymethyl, methylthio, dimethylcarboxamido, diethylcarboxamido and methylcarboxylate.

5. Use according to claim 1, wherein:
   - X is NZ,
   - Z is selected from the group consisting of hydrogen, methyl, ethyl, n-propyl and benzyl, and
   - R_1 is selected from the group consisting of methyl, ethyl, n-propyl and benzyl.

6. Use according to claim 1, wherein X is NZ and wherein the group NZ together with R_1 is selected from the group consisting of tetrahydropyridinyl, hydroxylamino, morpholinyl, piperidinyl, piperazinyl, 1,2,4-triazolyl and N-methylpiperazinyl.

7. Use according to claim 1, wherein the pteridine derivative is a compound selected from the group consisting of:
   - 2-amino-4-ethoxypteridine
   - 2-amino-4-ethoxy-6-chloro-pteridine
   - 2-amino-4-ethoxy-6-(4-methoxyphenyl)-pteridine
   - 2-amino-4-ethoxy-6-(2-methoxyphenyl)-pteridine
   - 2-amino-4-ethoxy-6-(3-methoxyphenyl)-pteridine
   - 2-amino-4-ethoxy-6-(3,4-difluorophenyl)-pteridine
   - 2-amino-4-ethoxy-6-(4-dimethylaminophenyl)-pteridine
   - 2-amino-4-ethoxy-6-(4-trifluoromethylphenyl)-pteridine
   - 2-amino-4-ethoxy-6-(2-thienyl)-pteridine

- 2-amino-4-ethoxy-6-(3-thienyl)-pteridine
- 2-amino-4-ethoxy-6-(3,4-dichlorophenyl)-pteridine
- 2-amino-4-ethoxy-6-(4-cyanophenyl)-pteridine
- 2-amino-4-ethoxy-6-(4-ethoxyphenyl)-pteridine
- 2-amino-4-ethoxy-6-(4-fluorophenyl)-pteridine
- 2-amino-4-ethoxy-6-(4-ethylphenyl)-pteridine
- 2-amino-4-ethoxy-6-(4-acetylphenyl)-pteridine
- 2-amino-4-ethoxy-6-(3-fluoro-4-methylphenyl)-pteridine
- 2-amino-4-ethoxy-6-(4-methylthiophenyl)-pteridine
- 2-amino-4-ethoxy-6-(4-N,N-dimethylbenzamido)-pteridine
- 2-amino-4-isopropoxypteridine
- 2-amino-4-isopropoxy-6-chloropteridine
- 2-amino-4-isopropoxy-6-(3-methyl-4-methoxyphenyl)-pteridine
- 2-amino-4-isopropoxy-6-(3,4-dimethylphenyl)-pteridine
- 2-amino-4-isopropoxy-6-(3-chloro-4-trifluoromethylphenyl)-pteridine
- 2-amino-4-isopropoxy-6-(3-chlorol-4-fluorophenyl)-pteridine
- 2-amino-4-isopropoxy-6-(4-N,N-diethylbenzamido)-pteridine
- 2-amino-4-isopropoxy-6-(4-trifluoromethylphenyl)-pteridine
- 2-amino-4-isopropoxy-6-(3,4-difluorophenyl)-pteridine
- 2-amino-4-isopropoxy-6-(4-methoxyphenyl)-pteridine
- 2-amino-4-isopropoxy-6-(4-ethoxyphenyl)-pteridine
- 2-amino-4-isopropoxy-6-(4-N,N-dimethylbenzamido)-pteridine
- 2-amino-4-isopropoxy-6-(3-thienyl)-pteridine
- 2-amino-4-isopropoxy-6-(4-cyanophenyl)-pteridine
- 2-amino-4-isopropoxy-6-(4-benzoic acid methyl ester)-pteridine
- 2-amino-4-isopropoxy-6-(4-acetylphenyl)-pteridine
- 2-amino-4-isopropoxy-6-(3,4-dimethoxyphenyl)-pteridine
- 2-amino-4-ethylthio-6-(3,4-dimethoxyphenyl)-pteridine
- 2-amino-4-isopropylthio-6-(3,4-dimethoxyphenyl)-pteridine
- 2-amino-4-pentoxy-6-styrylpteridine,
- 2-amino-4-n-pentoxy-6-(1,2-dibromo-2-phenylethyl)-pteridine,
- 2-amino-4-methoxy-6-styryl-7-methoxypteridine,
- 2-amino-4-dimethylamino-6-phenylpteridine,
- 2-amino-4-dimethylamino-6-(4-tolyl)pteridine,
- 2-amino-4-dimethylamino-6-(4-methoxyphenyl)pteridine,
- 2-amino-4-diethylamino-6-phenylpteridine,
- 2-amino-4-diethylamino-6-(4-chlorophenyl)pteridine.

- 2-amino-4-diethylamino-6-(4-methoxyphenyl)pteridine,
- 2-amino-4-diethylamino-6-(3,4-dimethoxyphenyl)pteridine,
- 2-amino-4-dipropylamino-6-phenylpteridine,
- 2-amino-4-dipropylamino-6-(4-chlorophenyl)pteridine,
- 2-amino-4-dipropylamino-6-(4-methoxyphenyl)pteridine,
- 2-amino-4-dipropylamino-6-(3,4-dimethoxyphenyl)pteridine,
- 2-amino-4-morpholino-6-phenylpteridine,
- 2-amino-4-morpholino-6-(4-chlorophenyl)pteridine,
- 2-amino-4-morpholino-6-(4-methoxyphenyl)pteridine,
- 2-amino-4-morpholino-6-(3,4-dimethoxyphenyl)pteridine,
- 2-amino-4-piperidino-6-phenylpteridine,
- 2-amino-4-piperidino-6-(4-chlorophenyl) pteridine,
- 2-amino-4-piperidino-6-(4-methoxyphenyl)pteridine,
- 2-amino-4-piperidino-6-(3,4-dimethoxyphenyl)pteridine,
- 2-amino-4-N-methylpiperazino-6-phenylpteridine,
- 2-amino-4-N-methylpiperazino-6-(4-chlorophenyl)pteridine,
- 2-amino-4-N-methylpiperazino-6-(4-methoxyphenyl)pteridine,
- 2-amino-4-methylpiperazino-6-(3,4-dimetnoxyphenyl)pteridine,
- 2-amino-4-pyrrolidino-6-(4-methoxyphenyl)pteridine,
- 2-amino-4-piperazino-6-phenylpteridine,
- 2-amino-4-piperazino-6-(4-chlorophenyl)pteridine,
- 2-amino-4-piperazino-6-(4-methoxyphenyl)pteridine,
- 2-amino-4-piperazino-6-(3,4-dimethoxyphenyl)pteridine,
- 2-amino-4-morpholino-6-(3,4,5-trimethoxyphenyl)pteridine,
- 2-amino-4-morpholino-6-(3,4-formylidene-3,4-dihydroxyphenyl)pteridine,
- 2-amino-4-dimethylamino-6-(3,4-formylidene-3,4-dihydroxyphenyl) pteridine,
- 2-amino-4-pyrrolidino-6-(3,4,dimethoxyphenyl)pteridine,
- 2-amino-4-dimethylamino-6-(3,4-dimethoxyphenyl)pteridine,
- 2-amino-4-dimethylamino-6-methylpteridine,
- 2-amino-4-ethoxy-6-phenylpteridine,
- 2-amino-4-propylamino-6-phenylpteridine,
- 2-amino-4-propylamino-6-(3,4-dimethoxyphenyl)pteridine,
- 2-acetamido-4-isopropoxy-6-(3,4-dimethoxyphenyl)pteridine,
- 2-amino-4-ethoxy-6-(3,4-dimethoxyphenyl)pteridine,
- 2-amino-4-(1,2,3,6-tetrahydropyridinyl)-6-(3,4-dimethoxyphenyl)pteridine,
- 2-amino-4-ethoxy-pteridine,
- 2-amino-4-ethoxypteridine-N^8-oxide,

- 2-amino-4-isopropoxypteridine-N^6-oxide,
- 2-amino-6-chloro-4-ethoxypteridine,
- 2-amino-6-chloro-4-isopropoxypteridine,
- 2-amino-6-(p-methoxyphenyl)-4-ethoxy-pteridine;
- 2-amino-6-(o-methoxyphenyl)-4-ethoxy-pteridine;
- 2-amino-6-(m-methoxyphenyl)-4-ethoxy-pteridine;
- 2-amino-6-(3,4-difluorophenyl)-4-ethoxy-pteridine;
- 2-amino-6-(p-dimethylaminophenyl)-4-ethoxy-pteridine;
- 2-amino-6-(p-trifluoromethylphenyl)-4-ethoxy-pteridine;
- 2-amino-6-(2-thienyl)-4-ethoxy-pteridine;
- 2-amino-6-(3-thienyl)-4-ethoxy-pteridine;
- 2-amino-6-(3,4-dichlorophenyl)-4-ethoxy-pteridine;
- 2-amino-6-(p-cyanophenyl)-4-ethoxy-pteridine;
- 2-amino-6-(p-ethoxyphenyl)-4-ethoxy-pteridine;
- 2-amino-6-(p-fluorophenyl)-4-ethoxy-pteridine;
- 2-amino-6-(p-ethylphenyl)-4-ethoxy-pteridine;
- 2-amino-6-(p-acetylphenyl)-4-ethoxy-pteridine;
- 2-amino-6-(3-methyl-4-fluorophenyl)-4-ethoxy-pteridine;
- 2-amino-6-(p-thiomethylphenyl)-4-ethoxy-pteridine;
- 2-amino-6-(p-N,N-dimethylbenzamido)-4-ethoxy-pteridine;
- 2-amino-6-(3,4-dimethoxyphenyl)-4-ethoxy-pteridine,
- 2-amino-6-(3-methyl-4-methoxyphenyl)-4-isopropoxypteridine;
- 2-amino-6-(3,4-dimethylphenyl)-4-isopropoxypteridine;
- 2-amino-6-(3-chloro-4-trifluoromethylphenyl)-4-isopropoxypteridine;
- 2-amino-6-(3-chloro-4-fluorophenyl)-4-isopropoxypteridine;
- 2-amino-6-(p-N,N-diethylbenzamido)-4-isopropoxypteridine;
- 2-amino-6-(p-trifluoromethylphenyl)-4-isopropoxypteridine;
- 2-amino-6-(3,4-difluorophenyl)-4-isopropoxypteridine;
- 2-amino-6-(p-methoxyphenyl)-4-isopropoxypteridine;
- 2-amino-6-(p-ethoxyphenyl)-4-isopropoxypteridine;
- 2-amino-6-(p-dimethylbenzamido)-4-isopropoxypteridine;
- 2-amino-6-(3-thienyl)-4-isopropoxypteridine;
- 2-amino-6-(p-cyanophenyl)-4-isopropoxypteridine;
- 2-amino-6-(p-benzoic acid methyl ester)-4-isopropoxypteridine;
- 2-amino-6-(p-acetylphenyl)-4-isopropoxypteridine;
- 2-amino-6-(3,4-dimethoxyphenyl)-4-isopropoxypteridine,
- 2-amino-4-mercaptoethyl-6-(3,4-dimethoxyphenyl) pteridine;

- 2-amino-4-mercaptoisopropyl-6-(3,4-dimethoxyphenyl) pteridine,
- 2-acetylamino-4-(1,2,4-triazolyl)-6-(p-methoxyphenyl) pteridine,
- 2-acetylamino-4-(1,2,4-triazolyl)-7-(p-methoxyphenyl)pteridine,
- 2-amino-4-isopropoxy-7-(p-methoxyphenyl) pteridine,
- 2-amino-4-isopropoxy-7-(3,4-dimethoxyphenyl) pteridine,
- 2-amino-4-ethoxy-7-(3,4-dimethoxyphenyl) pteridine,
- 2-amino-4-methoxy-7-(3,4-dimethoxyphenyl) pteridine,
- 2-amino-4-(1,2,3,6-tetrahydropyridinyl)-6-(3,4-dimethoxyphenyl)pteridine,
- 2-amino-4-(diethanolamino)-6-[[3,4-(dimethoxyphenyl)]pteridine,
- 2-amino-4-thiomorpholino-6-[[3,4-(dimethoxyphenyl)]pteridine,
- 2-amino-4-morpholino-6-(4-acetanilide) pteridine,
- 2-amino-4-morpholino-6-(3-acetanilide) pteridine,
- 2-amino-4-morpholino-6-(4-aminophenyl) pteridine,
- 2-amino-4-morpholino-6-(3-aminophenyl) pteridine,
- 2-amino-4-morpholino-6-(4-benzoylaminophenyl) pteridine;
- 2-amino-4-morpholino-6-(4-phenoxyacetylaminophenyl) pteridine;
- 2-amino-4-morpholino-6-(4-propionylaminophenyl) pteridine;
- 2-amino-4-morpholino-6-(4-furoylaminophenyl) pteridine;
- 2-amino-4-morpholino-6-(4-cyclohexanoylaminophenyl) pteridine;
- 2-amino-4-morpholino-6-[4-(4-chlorobenzoyl)aminophenyl] pteridine;
- 2-amino-4-morpholino-6-(4-benzyloxyacetylaminophenyl) pteridine,
- 2-amino-4-morpholino-6-(4-isonicotinoylaminophenyl) pteridine;
- 2-amino-4-morpholino-6-(4-naphtoylaminophenyl) pteridine;
- 2-amino-4-morpholino-6-(4-methylsulfonylaminophenyl) pteridine;
- 2-amino-4-morpholino-6-(4-ethylsuccinylaminophenyl) pteridine;
- 2-amino-4-morpholino-6-[4-(4-methylbenzoate)aminophenyl) pteridine;
- 2-amino-4-morpholino-6-(3-benzoylaminophenyl) pteridine;
- 2-amino-4-morpholino-6-(3-benzensulfonylaminophenyl) pteridine;
- 2-amino-4-morpholino-6-(3-phenoxyacetylaminophenyl) pteridine;
- 2-amino-4-morpholino-6-(3-isonicotinoylaminophenyl) pteridine;
- 2-amino-4-morpholino-6-(3-cyclohexanoylaminophenyl) pteridine;
- 2-amino-4-morpholino-6-[3-(4-methylbenzoate)aminophenyl] pteridine;
- 2-amino-4-morpholino-6-(3-ethylsuccinylaminophenyl) pteridine;
- 2-amino-4-morpholino-6-(3-ethylmalonylaminophenyl) pteridine;
- 2-amino-4-morpholino-6-(3-benzyloxyacetylaminophenyl) pteridine;
- 2-amino-4-morpholino-6-(3-ethylsulfonylaminophenyl)pteridine,
- 2-amino-4-morpholino-6-[3-Boc-(L)-phenylalanine-aminophenyl] pteridine;

- 2-amino-4-morpholino-6-[3-Boc-(D)-phenylalanine-aminophenyl] pteridine;
- 2-amino-4-morpholino-6-[3-Boc-(L)-tryptophane-aminophenyl] pteridine;
- 2-amino-4-morpholino-6-[3-Boc-(D)-tryptophane-aminophenyl] pteridine,
- 2-amino-4-morpholino-6-(4-hydroxyphenyl) pteridine,
- 2-amino-4-morpholino-6-(4-ethoxyphenyl) pteridine;
- 2-amino-4-morpholino-6-(4-benzyloxyphenyl) pteridine;
- 2-amino-4-morpholino-6-(4-(phenethyloxy)-phenyl) pteridine;
- 2-amino-4-morpholino-6-(4-phenoxy-butyronitrile) pteridine;
- 2-amino-4-morpholino-6-(4-propoxy-phenyl) pteridine;
- 2-amino-4-morpholino-6-(4-phenoxy-butyric acid ethyl ester) pteridine;
- 2-amino-4-morpholino-6-(4-phenoxy-acetic acid ethyl ester) pteridine
- 2-amino-4-morpholino-6-(4-(2-methoxyethoxy)-phenyl) pteridine; and
- 2-amino-4-morpholino-6-(4-butoxy-phenyl)-pteridine.